

Application Number: 10/602,456  
Balschmidt et al.  
Filed: June 23, 2003  
Attorney Docket No.: 6460.200-US  
Via Facsimile No.: 571-273-8300

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#### REMARKS

The examiner states in the Office Action Summary claims numbered 1-23 are pending in the application, and claims numbered 1-23 are rejected. The specification is amended herein. Claims numbered 2 and 12 are cancelled herein. Claims numbered 1, 3, 13 and 20-23 are amended herein. Following entry if this amendment, claims numbered 1, 3-11, and 13-23 are pending in the present application.

(1) The examiner states Applicant's submission of the IDS filed February 27, 2004 is incomplete because the non-patent reference "International Search Report Filed October 23, 2003", was not submitted with the PTO-1449 form.

Applicant regrets this oversight. A replacement PTO-1449 form and the cited reference are enclosed herewith.

#### Specification/Claims Objections

(2) The examiner has objected to the specification because the last page of the specification filed June 23, 2003, contains the claims 1-11. The specification and the claims should be set forth in separate sheets.

Applicant has amended the specification herein to begin the claims on a separate sheet, following the presently numbered page 9 of the specification. Applicant respectfully requests reconsideration and withdrawal of the objection to the specification.

(3) The examiner has objected to the specification page 2, line 28, stating the phrase "methylsulfonylmethane or MSM" should read "methylsulfonylmethane (MSM)."

Applicant has amended the specification herein to correct the above-identified phrase. Applicant respectfully requests reconsideration and withdrawal of the objection to the specification.

(4) The examiner has objected to the specification page 3, lines 20-21, and page 5, line 31, stating "GLP-1", "GLP-2", "Factor VII", "Factor VIII", and "HPLC", should be spelled out for

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the first instance of use.

Applicant has amended the specification herein to provide the complete form of the phrase represented by the abbreviations "GLP-1", "GLP-2", and "HPLC." However, Applicant respectfully submits "Factor VII" and "Factor VIII" are correctly set forth in their present form, as these phrases are not abbreviations. Applicant respectfully requests reconsideration and withdrawal of the objection to the specification.

(5) The examiner has objected to the specification page 6, lines 8-9, stating the phrase "Δ% Purity" should be clarified.

Applicant has amended the specification herein to provide clarification of the phrase "Δ% Purity." Applicant respectfully requests reconsideration and withdrawal of the objection to the specification.

(6) The examiner has objected to the specification stating the specification sets forth the peptide analogs e.g., *Lys(B28)Pro(B29)-human insulin*, without reciting the corresponding sequence identifier. Additionally, the terms "B28" and "B29" need to be clarified to indicate whether they refer to insulin B-chain residues 28 and 29.

Applicant respectfully submits sequence identifiers are not required for this application. Applicant directs the examiners attention to MPEP 2421.02, wherein the requirements of the sequence rules are summarized. Specifically paragraph 2, which states in part "The sequence rules embrace ...all unbranched, non-D amino acid sequences with four or more amino acids, *provided that there are at least 4 "specifically defined" ... amino acids*" (emphasis added). The present application does not disclose or claim amino acid sequences having 4 or more "specifically defined" amino acids. Furthermore, the amino acid sequences of human growth hormone, insulin, GLP-1, GLP-2, Factor VIIa, Factor VIII, EPO, glucagon, IL-2, interferon- $\alpha$  and interferon- $\beta$ , referred to in the specification, are known in the art and would not further the USPTO goals of building a comprehensive data base or properly assessing the prior art.

Applicant believes the meaning of the terms "B28" and "B29" is clear as stated. Applicant respectfully submits the terms "B28" and "B29" represent standard nomenclature used

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when referring to insulin, and these terms are readily understood by those familiar with the technology to be insulin B-chain amino acid residues number 28 and 29.

Applicant respectfully requests reconsideration and withdrawal of the objection to the specification.

(7) The examiner has objected to claims 2 and 3 stating the phrase "the amount of dimethyl sulfone" should be changed to "the concentration of dimethyl sulfone."

Applicant has cancelled claim 2, and made the recommended amendment to claim 3. Applicant respectfully requests reconsideration and withdrawal of the objection to claims 2 and 3.

(8) The examiner has objected to claims 12 and 15-23, stating the peptide analogues/derivatives, e.g., "Asp(B28)-human insulin", "Lys(B28) Pro(B29)-human insulin", " $N^{aB29}$ -tetradecanoyl des (B30)-human insulin", Gly(A21) Arg(B31)-human insulin ' $N^{eB29}$ -lithocholoyl- $\gamma$ -glutamyl des (B30)-human insulin", "Gly(8)-human GLP-1", "Arg(34), N- $\varepsilon$ -( $\gamma$ -Glu( $N$ - $\alpha$ -hexadecanoyl))-Lys(26)-human GLP-1(7-37)OH", and "Gly(2)-human GLP-2", lack the corresponding peptide primary structure and/or amino acid sequence identifiers.

Applicant respectfully asserts corresponding peptide primary structure and/or amino acid sequence identifiers are not required in the present application. Applicant directs the examiner's attention to Applicant's response in (6) above.

Applicant respectfully requests reconsideration and withdrawal of the objection to claims 12 and 15-23.

(9) The examiner has objected to claim 20, stating the term " $N^{eB29}$ -lithocholoyl- $\gamma$ -glutamyl des (B30)-human insulin", should be " $N^{aB29}$ -lithocholoyl- $\gamma$ -glutamyl des (B30)-human insulin."

Applicant has amended claim 20 to correct this typographical error. Applicant respectfully requests reconsideration and withdrawal of the objection to claim 20.

Claim Rejections – 35 U.S.C. § 112, second paragraph

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(10) The examiner has rejected claims numbered 12-23 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, in claim 12, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. Additionally, claim 12 recites "a derivative of any such peptide or analogue." The specification does not define the derivative of the peptide analogue. Not that on page 2, lines 22-24, the specification has defined the derivative as an analogue of the parent peptide; and thus, said recitation "derivative (analogue) of ... analogue" is awkward and indefinite.

Applicant has cancelled claim 12. However due to the amendment to claim 1, wherein the limitations found in claim 12 are added, Applicant will respond to the examiner's rejection. Applicant has removed the phrase "such as" from the language of the claim. Applicant respectfully disagrees with the examiner's assertion that the specification has defined the derivative as an analogue of the parent peptide. Page 2, lines 22-24 states: "The term "derivative" as used herein designates a peptide in which *one or more of the amino acid residues of the parent peptide or analogue of the parent peptide have been chemically modified*, eg by alkylation, acylation, ester formation or amide formation." (emphasis added) Applicant respectfully submits this definition is clearly set forth and the examiner's interpretation is incorrect. Applicant respectfully requests reconsideration and withdrawal of this rejection.

#### Claim Rejections – 35 U.S.C. § 102

(11) The examiner has rejected claims numbered 1 and 4-11 under 35 U.S.C. § 102 (b) as being anticipated by Jacob, E. (EP 1 052 288 A1).

Applicant has amended claim 1 to include additional limitations and respectfully submits the amendment obviates the examiner's rejection. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims numbered 1 and 4-11 under 35 U.S.C. § 102 (b).

(12) The examiner has rejected claims numbered 1, 4 and 6-12 under 35 U.S.C. § 102 (b) as

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being anticipated by Braun, S. (EP 1 254 961 A1).

Applicant has cancelled claim number 12. Applicant has amended claim 1 to include additional limitations and respectfully submits the amendment obviates the examiner's rejection.

Applicant respectfully requests reconsideration and withdrawal of the rejection of claims numbered 1, 4 and 6-12 under 35 U.S.C. § 102 (b).

(13) The examiner has rejected claims numbered 1-3 under 35 U.S.C. § 102 (a) as being anticipated by Marini, J. (U.S. 6,328,987).

Applicant has amended claim 1 to include additional limitations and respectfully submits the amendment obviates the examiner's rejection. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims numbered 1-3 under 35 U.S.C. § 102 (a).

#### Claim Rejections – 35 U.S.C. §§ 102/103

(14) The examiner has rejected claims numbered 1 and 4-11 under 35 U.S.C. § 102 (b) as being anticipated by, or in the alternative as obvious under 35 U.S.C. § 103 (a) over Herschler, R. (U.S. 4,559,329).

Applicant has amended claim 1 to include additional limitations and respectfully submits the amendment obviates the examiner's rejection. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims numbered 1 and 4-11 under 35 U.S.C. § 102 (b) as being anticipated by, or in the alternative as obvious under 35 U.S.C. § 103 (a).

(15) The examiner has rejected claims numbered 1-11 under 35 U.S.C. § 102 (b) as being anticipated by, or in the alternative as obvious under 35 U.S.C. § 103 (a) over Herschler, R. (U.S. 4,973,605).

Applicant has amended claim 1 to include additional limitations and respectfully submits the amendment obviates the examiner's rejection. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims numbered 1-11 under 35 U.S.C. § 102 (b) as being anticipated by, or in the alternative as obvious under 35 U.S.C. § 103 (a).

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#### Claim Rejections – 35 U.S.C. § 103

(16) The examiner has rejected claims numbered 1-23 under 35 U.S.C. § 103 (a) as being unpatentable over Herschler, R.J. (U.S. 4,973,605), taken with Herschler et al. (U.S. 3,551,554), Ertl et al. (U.S. 6,686,177), Brader et al. (U.S. 6,465,426), Habermann et al. (U.S. 6,534,288), Havelund et al. (U.S. 5,750,497), Knudsen et al. (U.S. 2001/0011071), Knudsen et al. (U.S. 6,939,853) and Drucker, D.J. (U.S. 5,952,301).

To further prosecution of the present application, Applicant has amended claim 1 to include additional limitations and respectfully submits the amendment obviates the examiner's rejection. However, Applicant respectfully disagrees with the examiner's assertion that the present claims are rendered obvious by the cited references. Applicant respectfully submits the Herschler references cited by the examiner (U.S. 3,551,554 and U.S. 4,973,605) are not references that are either in the field of the Applicants endeavor or reasonably pertinent to the specific problem with which the Applicant was involved. The Federal Circuit has stated that [a] reference is reasonably pertinent if ... it is one which, because of the matter with which it deals, logically would have commanded itself to the inventor's attention in considering his problem....If a reference disclosure has the same purpose as the claimed invention, the reference relates to the same problem....[I]f it is directed to a different purpose, the inventor would accordingly have had less motivation or occasion to consider it. *In re Clay*, 966 F.2d 656 (Fed. Cir. 1992). Applicant respectfully asserts enhancing tissue penetration of physiologically active agents with DMSO and the use of MSM to relieve pain and nocturnal cramps and to reduce stress-induced deaths in animals have little relevance to the use of MSM as an isotonicity agent for pharmaceutical compositions for parenteral administration.

Additionally, it appears the examiner has included separate references to represent the different features described in the claims of the instant application. The examiner has pieced together the claimed invention using Applicant's claimed invention as a guide. It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teaching of the prior art so that the claimed invention is rendered obvious. One cannot use hindsight reconstruction to pick and choose among disclosures in the prior art to

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deprecate the claimed invention. *In re Fine*, 823 F.2d 1071 (Fed. Cir. 1988). Applicant respectfully requests the examiner consider the claim as a whole.

Applicant respectfully requests reconsideration and withdrawal of the rejection of claims numbered 1-23 under 35 U.S.C. § 103 (a).

Applicant reserves the right to file continuing or divisional applications directed to non-elected and/or cancelled subject matter. The examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this response or application.

Respectfully submitted,



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